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BEFORE THE PATENT TRIAL AND APPEAL BOARD

Ex parte ROBERT C. AXTELL, LAWRENCE STEINMAN, MAY H. HAN, BRIGIT A. DE JONG, CHANDER RAMAN, MICHAEL WALKER, JING SHI, and TITO A. SERAFINI

Appeal 2015-003156
Application 13/026,181[1]
Technology Center 1600

Before DONALD E. ADAMS, RICHARD M. LEBOVITZ, and TAWEN CHANG, *Administrative Patent Judges*.

LEBOVITZ, *Administrative Patent Judge*.

DECISION ON APPEAL

This appeal involves claims directed to methods for assessing prognosis for responsiveness of a human multiple sclerosis patient to an IL-17 inhibitor. The Examiner rejected the claims under 35 U.S.C. § 101. We have jurisdiction under 35 U.S.C. § 134. We affirm and designate the affirmance of claims 14 and 15 a new ground of rejection.

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[1] The real party in interest is listed in the Appeal Brief as the Board of Trustees of the Leland Stanford Junior University.

STATEMENT OF THE CASE

The Examiner rejected claims 1, 14, 15, 19, and 43 under 35 U.S.C. § 101 as not directed to patent eligible subject matter. Final Rej. 2. Citing *Mayo Collaborative Services v. Prometheus Laboratories, Inc.*, 132 S.Ct. 1289 (2012), the Examiner determined that the claimed process is "a law of nature/natural principle," making it a judicial exception and ineligible for patenting under 35 U.S.C. § 101. *Id.*

There are two independent claims, claims 1 and 19. Claim 1 is representative and reads as follows:

> 1. A method for assessing prognosis for responsiveness of a human multiple sclerosis patient to an IL-17 inhibitor, comprising:
>
> analyzing a blood sample from said patient with an antibody-based assay for the presence of IL-17F and IL-7 to provide a quantitative dataset for IL-17F and IL-7 to detect whether altered levels of IL-17F and IL-7 relative to a control are present;
>
> assessing responsiveness to an IL-17 inhibitor by comparing the quantitative dataset for IL-7 and IL-17F to a control dataset, wherein increased levels of IL-17F and decreased levels of IL[-]7 relative to a control indicates that the patient is responsive to an IL-17 inhibitor; and
>
> providing to the multiple sclerosis patient an assessment of the prognosis for responsiveness to an IL-17 inhibitor.

App. Br. 14 (Claims Appendix).

Claim 19 involves the same steps. Thus, the analysis for claim 1 applies equally to claim 19.

SECTION 101 REJECTION

Since *Mayo*, a two-step for patent eligibility under Section 101 has emerged. As set forth in *Alice Corp. Pty. Ltd. v. CLS Bank Int'l*, 134 S.Ct. 2347, 2355 (2014):

> First, we determine whether the claims at issue are directed to one of those patent-ineligible concepts [*e.g.,* a law of nature, natural phenomenon, or abstract idea]. If so, we then ask, what else is there in the claims before us? . . . We have described step two of this analysis as a search for an inventive concept—i.e., an element or combination of elements that is sufficient to ensure that the patent in practice amounts to significantly more than a patent upon the ineligible concept itself.

Id. (alterations, citations, and quotation marks omitted).

With respect to the first step, in *Mayo*, the Supreme Court considered method claims that required analysis of metabolites in the blood of a patient being treated with a thiopurine drug to determine the likelihood that the patient could suffer toxic side effects from particular doses of the drug. *Mayo*, 132 S.Ct. at 1296–9. The Court concluded that "the claims were necessarily directed to an underlying law of nature or natural phenomenon, even if implementation of the method involves substantial human labor and ingenuity." *Genetic Technologies Ltd. v. Merial L.L.C.*, 818 F.3d 1369, 1275 (Fed. Cir. 2016). The *Mayo* Court stated:

> While it takes a human action (the administration of a thiopurine drug) to trigger a manifestation of this relation in a particular person, the relation itself exists in principle apart from any human action. The relation is a consequence of the ways in which thiopurine compounds are metabolized by the body—entirely natural processes. And so a patent that simply describes that relation sets forth a natural law.

Mayo, 132 S.Ct. at 1297.

Claim 1 is directed to a "method for assessing prognosis for responsiveness of a human multiple sclerosis patient to an IL-17 inhibitor." The assessment is accomplished by detecting IL-17F and IL-7 in a blood sample. IL-17F and IL-7 are cytokines that are found naturally in the blood. Spec. 7. The detected amounts are compared to a "control dataset." The claim states that "increased levels of IL-17F and decreased levels of IL[-]7 relative to a control indicates that the patient is responsive to an IL-17 inhibitor." Thus, the information on natural levels of cytokines is used to predict whether a patient will respond to an IL-17 inhibitor. The final step of the method provides the information on cytokine levels to a multiple sclerosis patient as "an assessment of the prognosis for responsiveness to an IL-17 inhibitor."

The levels of IL-17F and IL-7 recited in claim 1 are a "natural phenomenon" because they are a snapshot of the natural blood levels of the cytokines found in a multiple sclerosis patient. The method involves detecting the natural presence of these cytokines in a blood sample obtained from the patient. The subsequent step of "assessing responsiveness to an IL-17 inhibitor" by comparing the cytokine levels to control levels is a correlation step that describes the natural disease status of the patient. While the discovered relationship between the cytokine levels and the responsiveness to an IL-17 inhibitor might be new, the claim simply characterizes a "discovered fact about . . . biology" and therefore is a natural law. *Genetic Technologies*, 818 F.3d at 1376. As a consequence, we conclude claim 1 is directed to patent ineligible subject matter under the first part of the *Mayo/Alice* test.

The second part of the test asks whether the claims contain an "inventive concept" sufficient to transform the claimed law of nature into patent-eligible subject matter. *Id.*

> "The question ... is whether the claims do significantly more than simply describe [a] natural relation[ ]", 132 S.Ct. at 1297. The inventive concept necessary at step two *Mayo* of the *Mayo/Alice* analysis cannot be furnished by the unpatentable law of nature (or natural phenomenon or abstract idea) itself. That is, under *the Mayo/Alice* framework, a claim directed to a newly discovered law of nature (or natural phenomenon or abstract idea) cannot rely on the novelty of that discovery for the inventive concept necessary for patent eligibility; instead, the application must provide something inventive, beyond mere "well-understood, routine, conventional activity." *Mayo*, 132 S.Ct. at 1294; see also *Myriad*, 133 S.Ct. at 2117; *Ariosa*, 788 F.3d at 1379. "[S]imply appending conventional steps, specified at a high level of generality, to laws of nature, natural phenomena, and abstract ideas cannot make those laws, phenomena, and ideas patentable." *Mayo*, 132 S.Ct. at 1300. Claims directed to laws of nature are ineligible for patent protection when, "(apart from the natural laws themselves) [they] involve well-understood, routine, conventional activity previously engaged in by researchers in the field." *Mayo*, 132 S.Ct. at 1294.

Id.

In this case, we have not been directed to evidence that the steps of claim 1 in analyzing the cytokine levels using an antibody-based test adds anything to the routine technology conventionally used to characterize cytokines.

Appellants attempt to distinguish *Mayo* because of the "wherein" clauses which Appellants state "were not integrated into the claim and,

therefore, did not apply, rely on, or use any natural principle." Appeal Br. 6 and 12 (Factor (j)). Appellants contend:

> For example, the 'wherein' clauses of the *Mayo* claim contained the phrase "indicates a need to," which did not actually require anything of the one performing the method and instead simply stated the law itself. In other words, the 'wherein' clauses of *Mayo* were not associated with any step in particular, but were instead tacked on to the claim as a whole, and the clauses did not require any kind of a step to be taken when performing the method. This lack of integration was critical because it meant that the 'wherein' clauses provided no actual limitations to the claims. Thus, the analysis of the *Mayo* claim did not give weight to the 'wherein' clauses because the 'wherein' clauses were not limiting. In other words, the analysis of the *Mayo* claim took into account all limitations of the claim, and the 'wherein' clauses could be ignored because they provided no limitations. The only steps that provided actual limitations (steps (a) and (b)) were in fact routinely carried out in the art, in the same exact order, in the same patient population, and even for the same purpose.

Appeal Br. 6.

We do not agree. The *Mayo* Court explicitly characterized the "wherein" clause as a step in the claim and considered it as an integral part of the claim.

> What else is there in the claims before us? The process that each claim recites tells doctors interested in the subject about the correlations that the researchers discovered. In doing so, it recites an "administering" step, a "determining" step, and a "wherein" step. These additional steps are not themselves natural laws but neither are they sufficient to transform the nature of the claim.

Mayo at 1297.

The Court found that "the 'wherein' clauses simply tell a doctor about the relevant natural laws, at most adding a suggestion that he should take

those laws into account when treating his patient." *Id.* Consequently, we are not persuaded by Appellants' argument that the "wherein" clauses were ignored by the *Mayo* Court. Rather, the Court looked at the claim as a whole and decided that the claim set forth "laws of nature" because the relationship between the blood levels and the drug "itself exists in principle apart from any human action. The relation is a consequence of the ways in which thiopurine compounds are metabolized by the body—entirely natural processes." *Id.*

The claim in this appeal has the same issue. The blood levels of the cytokines predict whether a patent will be responsive to a drug – in a similar fashion to how metabolite blood levels in *Mayo* predicted whether a dosage of a drug would be effective or cause harm. *Id.* at 1296.

Once the *Mayo* Court saw that the claim is directed to a relationship setting forth a law of nature, the Court looked at the additional steps in the claim to determine whether the claim as whole was directed to ineligible subject matter. The Court held:

> The upshot is that the three steps ["administering," "wherein", "determining" *id.* at 1297] simply tell doctors to gather data from which they may draw an inference in light of the correlations. To put the matter more succinctly, the claims inform a relevant audience about certain laws of nature; any additional steps consist of well-understood, routine, conventional activity already engaged in by the scientific community; and those steps, when viewed as a whole, add nothing significant beyond the sum of their parts taken separately. For these reasons we believe that the steps are not sufficient to transform unpatentable natural correlations into patentable applications of those regularities.

Id. at 1298.

Consequently, we are not persuaded by Appellants' argument that claim 1 is distinguished from *Mayo* because all steps of the claim are "integrated" into the recited method. Appeal Br. 6.

Appellants discuss various factors which they argue militate against a finding of patent ineligibility. For example, Appellants contend that the claims do not pre-empt all uses of the relationship between the recited cytokines and drug responsiveness because the claims are limited to detecting the cytokines by an antibody based assay. *Id.* at 9 and 12 (Factor (i)).

In our opinion, narrowing the method by which the detection is accomplished does not change the patent eligibility of the claim because the method is still drawn to known and conventional technology utilized by scientists to measure cytokines. The issue is whether utilizing a known antibody detection method *transforms* the law of nature into patent eligible subject matter. The answer is "no" because the claim still reads on applying a natural phenomenon, using conventional technology, to make an inference about the disease status of a patient, which the *Mayo* Court found to be an ineligible application of a natural law under 35 U.S.C. § 101.

Appellants argue that the claim is directed to practical and significant application for the prognosis of multiple sclerosis. *Id.* at 9 and 10. This argument is not persuasive. The determination of drug toxicity in *Mayo* could also be said to have practical and significant applications. However, this fact was not determinative because the claim still relied on a natural law to make this determination. The principle which led the *Mayo* Court to invalidate the claim under 35 U.S.C. § 101 was not lack of a practical utility. Instead, the Court found a judicial exception to patent eligible subject matter

when the novelty of the claim was the discovery of a natural, biological principle and phenomenon, the same situation which characterizes the claims in this present appeal.

Appellants assert that the claim is "clearly an important and practical application of the alleged natural correlation because it provides guidance as to how a person may choose to live their life." *Id.* at 10. However, exactly for this reason, the Court found the claimed subject matter to constitute a judicial exception because *health* decisions about how to live one's life are not eligible for patent protection when a biological natural principle is at the core of the claim.

Appellants contend that "the claimed elements do more than describe the natural principle with general instructions to apply." *Id.* (Factor (d)). Appellants have not directed us to an element of the claim which goes beyond the general instruction to apply the discovered relationship between cytokines and drug response. Similarly, we do not see how quantitating a signal (*id.* (Factor (e)) is any different than measuring metabolite levels in *Mayo*.

The claims require measuring IL-17F and IL-7. Appellants contend that the Examiner did not establish that it was routine or conventional to perform these steps. *Id.* at 11. In response, the Examiner cited U.S. Pat. Pubs. 2009/0317400 (publ. Dec. 24, 2009) and 2010/0040616 (publ., Feb. 18, 2010) to establish that it was known prior to the invention to measure the recited cytokines in a sample. Ans. 18. It is not disputed by the Examiner that the inventors discovered that the information about the cytokine levels was useful to indicate whether a patient is responsive to an IL-17 inhibitor.

But this discovery is no different from the one in *Mayo* where the inventors had discovered that certain metabolite levels predicted the toxicity of a drug.

For the foregoing reasons, we conclude that claim 1 is a judicial exception to patent eligibility under 35 U.S.C. § 101. For the same reason, we conclude that claim 19, and dependent claim 43, are also not eligible subject matter.

Claims 14 and 15

Claim 14 depends from claim 1 and further recites "administering an IL-17 inhibitor to a patient assessed as a responder to IL-17 inhibitors." Claim 15, depends from claim 14, and recites a specific inhibitor. The Examiner found that the claims are directed to patent ineligible subject matter.

As discussed above, there is a two-step analysis for determining whether a claim is patent ineligible. Even when the first step is met, as here for claim 1, there is a second part to the test. That second step is described in *Alice,* 134 S.Ct. at 2355, as follows:

> We have described step two of this analysis as a search for an inventive concept—i.e., an element or combination of elements that is sufficient to ensure that the patent in practice amounts to significantly more than a patent upon the ineligible concept itself.

We interpret claim 14 to require administration of an IL-17 inhibitor to a multiple sclerosis ("MS") patient. However, the administration of an IL-17 inhibitor to an MS patient was known prior to the filing date of the application at issue in this appeal. Spec. ¶ 3. The Specification of the application discloses that IFN-β, a commercially available drug used to treat

MS, is an IL-17 inhibitor.[2] *Id.*, ¶¶ 3, 218, 243. The inventors state in the Specification that they discovered how to predict whether a patient will respond to IFN-β based on the IL-7/IL-17 profile. *Id.*, ¶ 278. In other words, the inventors have discovered how a natural biological law – the specific naturally-occurring cytokines levels in patient – can be used to predict the efficacy of an "old" drug in treating multiple sclerosis in a patient. The administration step is therefore not "significantly more than . . . the ineligible concept itself" (*Alice,* 134 S.Ct. at 2355) because administration of an IL-17 inhibitor, namely IFN-β, to an MS patient, had been practiced in the art prior to the application filing date. The "administering" step of the known drug, coupled with the "analyzing" and "assessing" steps, does not transform the patent eligibility of the claim because it simply informs a clinician to administer the same drug to the same class of patients when the natural law is satisfied.

While it is true that administration of the IL-17 inhibitor requires human action, the *Mayo* court considered the same type of activity and determined that it was insufficient to impart patent eligibility to the claim. Specifically, the patent claim in *Mayo* had a step in which levels of a drug metabolite were measured and then used to determine whether the amount of the drug administered to the patient should be increased or decreased ("'wherein the level of 6–thioguanine greater than about 400 pmol per $8x10^8$ red blood cells indicates a need to decrease the amount of said drug subsequently administered to said subject'"). *Mayo*, 132 S.Ct. at 1295. The

[2] The claim does not require recognition that the drug is an IL-17 inhibitor. While the claim may include IL-17 inhibitors not previously known to treat MS, the claim encompasses administering IFN-β, which is an "old" drug.

Court stated that "the 'wherein' clauses simply tell a doctor about the relevant natural laws, at most adding a suggestion that he should take those laws into account when treating his patient. . . . [T]hese clauses tell the relevant audience about the laws while trusting them to use those laws appropriately where they are relevant to their decisionmaking." *Id.*, 1297.

We discern no difference here. The "assessing" step of claim 1 tells a doctor about the natural law concerning cytokine levels in a patient diagnosed with MS that would be relevant when treating the patient. The subsequent "administering" step of claim 14 simply directs the doctor to take that law into consideration when treating the patient with the known IL-17 inhibitor IFN-β.

Our conclusion is not changed by Example 29 of the "Subject Matter Eligibility Examples: Life Sciences," dated May 2016, said to be used in conjunction with the *2014 Interim Guidance on Subject Matter Eligibility* (2014 IEG). Claim 2 in Example 29 is a diagnostic claim involving antibody detection and followed by diagnosis of the disease ("julitis") based on the presence of detected antibodies (*id.*, p. 10). Claim 2 was determined to be patent ineligible because the recited correlation between antibodies and disease was considered to be a consequence of natural processes (*id.*, p. 12). Claim 1 in this appeal has the same ineligibility deficit as in claim 2 of Example 29.

Claim 6 of Example 29 has an additional administering step in which anti-TNF antibody is administered to treat the diagnosed patient (*id.*, p. 11). The administration of anti-TNF antibody "to treat a patient diagnosed with julitis" was determined to be "well-understood, routine and conventional" (*id.*, 15). However, it was found that the claim was eligible for a patent

under 35 U.S.C. § 101 because "the combination of steps, which is not routine and conventional, ensures that patients who have julitis will be accurately diagnosed (due to the detection of JUL-1 in their plasma) and properly treated with anti-TNF antibodies, as opposed to being misdiagnosed as having rosacea as was previously commonplace" (*id.*).

The steps recited in rejected claim 14, however, do not ensure accurate differential diagnosis between two diseases as they did in claim 6 of Example 29. Rather, claim 14 involves administering a known drug to the same class of accurately diagnosed patients. The patients are the same; the drug is the same; the only difference is the knowledge of the natural law which enables a doctor to administer the drug to patients responsive to the drug. However, at least for the IL-17 inhibitor which is IFN-β, it is not new to administer the inhibitor to MS patients. As in *Mayo*, the administering step adds "conventional activity already engaged in by the scientific community," which is "not sufficient to transform unpatentable natural correlations into patentable applications of those regularities." *Mayo*, 132 S.Ct. at 1298.

For the foregoing reasons, we affirm the rejection of claim 14. Claim 15 was not separately argued, and thus falls with claim 14. See 37 C.F.R. 41.37(c)(1)(iv).

Because our rationale differs from the Examiner's, we designate the affirmance as it relates to claims 14 and 15 as a new ground of rejection pursuant to 37 C.F.R. 41.50(b).

SUMMARY

The § 101 rejection of claims 1, 14, 15, 19, and 43 is affirmed.

NEW GROUNDS OF REJECTION

When the Board designates a new ground of rejection under 37 C.F.R. § 41.50(b), the Appellants, as to each claim so rejected, have the option of:

(A) reopening prosecution before the Examiner by submitting an appropriate amendment and/or new evidence (37 C.F.R. § 41.50(b) (1)); or

(B) requesting rehearing before the Board (37 C.F.R. § 41.50(b) (2)).

The amendment and/or new evidence under 37 C.F.R. § 41.50(b) (1), or the request for rehearing under 37 C.F.R. § 41.50(b) (2), must be filed within 2 months from the date of the Board's decision. In accordance with 37 C.F.R. § 41.50(f), this 2-month time period may not be extended by the filing of a petition and fee under 37 C.F.R. § 1.136(a), but only under the provisions of 37 C.F.R. § 1.136(b).

AFFIRMED; § 41.50(b)